

Lo Yuk Ming Dennis, *et al.*  
Application No.: 09/944,951  
Page 3

**PATENT**

### **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application.

#### **Listing of the Claims**

Claim 1 (currently amended): A method for differentiating DNA species originating from cells of different individuals in a biological sample, the method comprising the ~~step~~ steps of:

(a) obtaining from one of the individuals a biological sample comprising the DNA species originating from the cells of different individuals; and

(b) determining epigenetic differences detecting a methylation difference between these the DNA species,

wherein detection of the methylation difference indicates DNA species from different individuals.

Claim 2 (currently amended): A method according to claim 1 wherein the ~~epigenetic difference is a difference in DNA methylation~~ biological sample is a fluid or cellular sample or a mixture thereof.

Claim 3 (original): A method according to claim 1 wherein the biological sample is plasma or serum.

Claim 4 (original): A method according to claim 1 wherein the biological sample is blood.

Claim 5 (original): A method according to claim 1 wherein one of the individuals is a pregnant female and the other individual is an unborn fetus.

Lo Yuk Ming Dennis, *et al.*  
Application No.: 09/944,951  
Page 4

PATENT

Claim 6 (original): A method according to claim 1 wherein one of the individuals is a transplantation recipient and the other individual is an organ donor.

Claim 7 (original): A method according to claim 6 wherein the transplantation is a bone marrow transplantation.

Claim 8 (currently amended): A method according to claim 1 further comprising the step of:

(c) ~~measuring concentrations~~ the concentration of the DNA species ~~having an epigenetic difference.~~

Claim 9 (canceled)

Claim 10 (currently amended): A method according to claim 2, further comprising the step of:

(c) ~~adding sodium bisulfite to the biological sample or to the DNA species to detect a DNA methylation difference.~~

Claim 11 (currently amended): A method according to claim 2, further comprising the step of:

(c) ~~performing a methylation-specific polymerase chain reaction to detect a DNA methylation difference.~~

Claim 12 (currently amended): A method according to claim ~~16~~ 1 further comprising the ~~step~~ steps of:

(c) amplifying the DNA species to generate a PCR product; and

Lo Yuk Ming Dennis, *et al.*  
Application No.: 09/944,951  
Page 5

PATENT

(d) sequencing ~~DNA to detect a DNA methylation difference~~ the PCR product.

Claim 13 (currently amended): A method according to claim 10 ~~1~~ further comprising the step of:

(c) performing primer extension to ~~detect a DNA methylation difference~~.

Claim 14 (original): A method according to claim 5 wherein the biological sample is maternal plasma or serum.

Claim 15 (currently amended): A method according to claim 14 further comprising the step of:

(c) measuring the concentration of fetal DNA in maternal plasma or serum.

Claim 16 (original): A method according to claim 15 wherein the concentration of fetal DNA measured is used to predict, monitor or diagnose or prognosticate a disorder.

Claim 17 (currently amended): A method according to claim 5 wherein ~~an epigenetic mark~~ the methylation difference is associated with a fetal or maternal disorder.

Claim 18 (original): A method according to claim 17 wherein the disorder is a chromosomal aneuploidy.

Claim 19 (original): A method according to claim 18 wherein the chromosomal aneuploidy is trisomy 21 (Down syndrome).

Lo Yuk Ming Dennis, *et al.*  
Application No.: 09/944,951  
Page 6

PATENT

Claim 20 (original): A method according to claim 17 wherein the disorder is preeclampsia.

Claim 21 (original): A method according to claim 17 wherein the disorder is an imprinting disorder.

Claim 22 (currently amended): A method according to claim 17 wherein the disorder is Prader-Willi syndrome.

Claim 23 (currently amended): A method according to claim 17 wherein the disorder is Angelman syndrome.

Claim 24 (currently amended): A method according to claim 14 wherein an epigenetic the methylation difference detected in fetal cells ~~in the placenta~~ is used as a fetus-specific marker ~~in maternal plasma or serum~~.

Claim 25 (currently amended): A method according to claim 6 further comprising the step of:

(c) measuring the ~~concentrations~~ concentration of organ donor and transplantation recipient DNA.

Claim 26 (currently amended): A method according to claim 25 wherein the ~~measurements~~ concentration of organ donor and transplantation recipient DNA are used to predict the clinical progress of the transplantation recipient.

Claim 27 (currently amended): A method according to claim 1 wherein one ~~individual~~ of the individuals is male and the other individual is female.

Lo Yuk Ming Dennis, *et al.*  
Application No.: 09/944,951  
Page 7

PATENT

Claim 28 (currently amended): A method according to claim 27 wherein the ~~epigenetic marker~~ methylation difference is detected on an inactivated X chromosome of the female individual.

Claim 29 (currently amended): A method according to claim 28 wherein a methylated DNA sequences sequence on the inactivated X chromosome are is sed to detect DNA originating from the female individual.

Claim 30 (currently amended): A method according to claim 1 wherein the ~~epigenetic differences are~~ methylation difference is analyzed inside cells.

Claim 31 (currently amended): A method according to claim 30 wherein the ~~epigenetic differences are~~ methylation difference is analyzed using in-situ methylation-specific polymerase chain reaction.

Claim 32 (currently amended): A method according to claim 1 wherein the ~~epigenetic differences are~~ methylation difference is used to sort or isolate cells from the individuals.

Claim 33 (currently amended): A method according to claim 1 wherein the ~~epigenetic differences are~~ methylation difference is used to purify DNA from the individuals.

Claim 34 (withdrawn): A kit for differentiating DNA species originating from different individuals in a biological sample comprising one or more reagents for ascertaining the methylation status of a species of DNA.

Lo Yuk Ming Dennis, *et al.*  
Application No.: 09/944,951  
Page 8

PATENT

Claim 35 (withdrawn): A kit according to claim 34 wherein the reagent for ascertaining the methylation status of the maternal DNA is sodium bisulfite

Claim 36 (withdrawn): A kit according to claim 34 further comprising one or more reagents for detecting the presence of DNA.

Claim 37 (withdrawn): A kit according to claim 34 further comprising one or more reagents for amplifying the amount of DNA present in the biological sample.

Claim 38 (withdrawn): A kit according to claim 34 further comprising one or more apparatuses for obtaining a DNA sample.

Claim 39 (new): A method according to claim 5 wherein the methylation difference is detected in fetal cells in the placenta.